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Documents Attached:

For: S/N 10/731,581, filed December 9, 2003, Docket No. R0148B-REG
Inventors Robert Than Hendricks, et al.

1. Transmittal Form
2. Supplemental IDS
3. Exhibits A, B and C

Doc 120000

PTO/SB/21 (08-03)

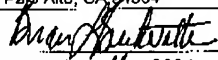
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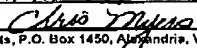
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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/731,581
	Filing Date	December 9, 2003
	First Named Inventor	Hondricks, Robert Than
	Art Unit	1632
	Examiner Name	TBA
Total Number of Pages In This Submission	Attorney Docket Number	R0148B-REG

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Firm or Individual name	ROCHE PALO ALTO LLC Patent Department, M/S A2-250 3431 Hillview Avenue, Palo Alto, CA 94304
Signature	 BRIAN L. BUCKWALTER, Reg. No. 46,585
Date	November 11, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Address to: Commissioner for Patents PO Box 1450 Alexandria, VA 22313 FAX to: 703-872-9306	First Inventor(s).	Hendricks, Robert Than
	Application Number	10/731,581
	Filing Date	12/9/2003
	Group Art Unit	1632
	Examiner	TBA
	Attorney Docket No.	R0148B-RFG
	Title:	ANTIVIRAL NUCLEOSIDE DERIVATIVES

Assistant Commissioner for Patents
Washington, D.C. 20231

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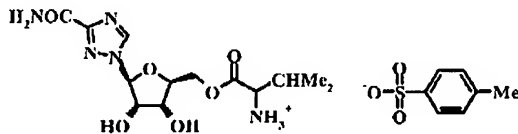
SUPPLEMENTARY INFORMATION DISCLOSURE STATEMENT

In recognition of the duty under 37 CFR §1.56, to disclose all information material to patentability the following facts and supporting documentation which have been communicated to Applicant's representative are hereby brought to the attention of the Examiner. This information is filed within three (3) months of the filing date of the application and therefore no fee is believed to be due; however, should this not be the case, the Commissioner is hereby authorized to charge any additional fees that may be required to Deposit Account No. 18-1700.

The Examiner is respectfully requested to consider these documents and to make them of record in the subject application.

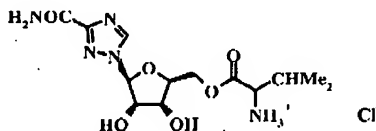
1. The present invention relates to prodrugs of the nucleoside compound, Levovirin. Levovirin was discovered by Valcant Pharmaceuticals (formerly ICN Pharmaceuticals) and licensed to Roche Pharmaceuticals.
2. U. S. Patent No. 6,552,183 contains composition of matter and composition claims to levovirin. U. S. Patent No. 6,495,677 contains composition of matter and composition claims to levovirin prodrugs. Among the compounds which are disclosed generically are 5'- α -aminoacyl compounds. No examples were disclosed in the specification. The inventors on these applications are or were employees of ICN Pharmaceuticals.
3. In early January of 2002, a sample of the tosylate salt of the valine ester of levovirin (I) was received by an individual at the Roche facility in Nutley NJ by Valcant Pharmaceuticals. The samples were accompanied by a sheet of paper with the structures. No other information was received at that time. (EXHIBIT A) A sample of the tosylate salt of the corresponding alanine ester also was received. The sample

was analyzed by scientists at Nutley by mass spectrometry and nuclear magnetic resonance spectroscopy and the data was consistent with that structure.



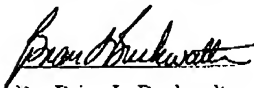
I

4. In meetings between Valeant and Roche personnel, Valeant provided sample submission forms for the tosylate salts of the valine, alanine and lysine esters of levovirin (EXHIBIT B). The forms indicate they were submitted on 3/27/2001, 3/22/2001 and 3/25/2001 respectively.
5. In meetings between Valeant and Roche, Valeant personnel indicated that the preparation of the tosylate salt was an important to obtain satisfactory material for manufacturing and formulation. EXHIBIT C is a copy of two Power Point slides shown by Valeant at planning meetings with Roche personnel which I received from Roche personnel and which I believe were provided to Roche personnel by Valeant.
6. Chemists at Roche Palo Alto I.L.C have been unable to prepare the tosylate salt I as a satisfactory crystalline non-hygroscopic solid. After considerable experimentation, the hydrochloride salt II was isolated as a dense crystalline solid which was available in good yield and whose physical properties were suitable for further handling and formulation.



II

Respectfully submitted,



By: Brian L. Buckwalter
Registration No. 46,585
Agent for Applicants

November __/__/2004

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